In Vivo Clonal Analysis Reveals Lineage-Restricted Progenitor Characteristics in Mammalian Kidney Development, Maintenance, and Regeneration.

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Public Summary:

Dr. Rinkevich in collaboration with Dr. Benjamin Dekel from the Tel-Aviv University in Israel, has looked into the mechanism and magnitude by which the mammalian kidney forms new proximal tubules, distal tubules, and collecting ducts segments (the tissues involved in all kidney functions). Here we utilized mouse genetic systems to permanently (genetically) label individual kidney cells from as when through embryonic development and following kidney damage. We show that the adult mammalian kidney undergoes continuous formation of new tubules, the functional kidney tissues, throughout life. By culturing individual renal epithelial cells, Dr. Rinkevich showed kidney tubules develop in culture, outside of the mouse, from individual cells that form distinct types of tubules. Furthermore, Dr. Rinkevich has shown that adult kidneys recovering from damage form tubules inside the mouse through expansions of single cells that form distinct tubule types. Dr. Rinkevich has shown the individual cells that form new kidney tubules are responsive to a protein called Wnt and could be identified on this basis. Collectively, these results indicate that the mammalian kidney tissues are constantly maintained and self-preserves by these unique cells.

Scientific Abstract:

The mechanism and magnitude by which the mammalian kidney generates and maintains its proximal tubules, distal tubules, and collecting ducts remain controversial. Here, we use long-term in vivo genetic lineage tracing and clonal analysis of individual cells from kidneys undergoing development, maintenance, and regeneration. We show that the adult mammalian kidney undergoes continuous tubulogenesis via expansions of fate-restricted clones. Kidneys recovering from damage undergo tubulogenesis through expansions of clones with segment-specific borders, and renal spheres developing in vitro from individual cells maintain distinct, segment-specific fates. Analysis of mice derived by transfer of color-marked embryonic stem cells (ESCs) into uncolored blastocysts demonstrates that nephrons are polyclonal, developing from expansions of singly fated clones. Finally, we show that adult renal clones are derived from Wnt-responsive precursors, and their tracing in vivo generates tubules that are segment specific. Collectively, these analyses demonstrate that fate-restricted precursors functioning as unipotent progenitors continuously maintain and self-preserve the mouse kidney throughout life.